ANALYTICAL AND SYNTHETIC INVESTIGATIONS IN OLEFINIC COMPOUNDS

1. Introduction

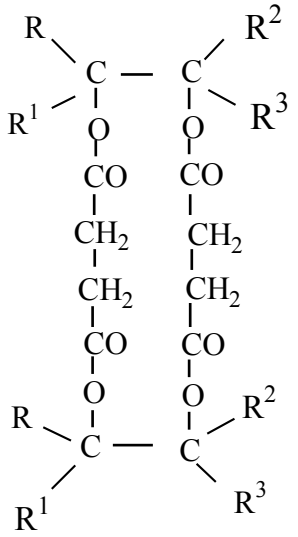
The syn-hydroxylation of olefins to 1, 2-diols first reported early last century is one of the most useful oxidation reactions. The dihydroxylation of olefins has been of value in degradation studies of natural products, in synthetic procedures, and in characterization of many olefinic compounds. At present 1, 2-diols are manufactured industrially by a two step sequence consisting of epoxidation of an olefin with a hydroperoxide or peroxide followed by hydrolysis of the resulting epoxide. Compared with this process the dihydroxylation of C=C double bond constitutes a more atom efficient and shorter route to 1, 2-diols. 1, 2-diols find a wide variety of applications in the fine chemical industry and as polyester monomers and antifreeze agents.

Chiral 1, 2-diols are employed as intermediates for pharmaceuticals and agrochemicals. Chiral molecules constitute the fundamental building blocks of much of biology. In general, only one enantiomer of a drug, agrochemical, flavoring agent or other molecule, when asymmetric, has the desired biological effect, while the other enantiomer has very different effect, or at least, places a metabolic burden on the body. For this reason, asymmetric synthesis to produce only one enantiomer of a molecule for such uses is extremely important. Thus finding new methods of asymmetric synthesis has in the past twenty or thirty years become a key activity for organic chemists.

All the methods currently available for asymmetric synthesis of 1, 2-diols from olefins involve the use of osmium reagents. Thus 0.2-0.4 mol% of osmium reagents, added to the reaction mixture either as osmium tetroxide or as the nonvolatile $K_2OsO_2(OH)_4$ are required for most olefinic substrates. From an industrial viewpoint, the high cost of osmium catalyst and chiral ligand as well as the toxicity and volatility of osmium tetroxide are the obstacles to large scale applications.

In this context it was one of our objectives to explore the possibility of hydroxylating olefinic compounds to chiral 1, 2-diols without using osmium reagents. An exhaustive investigation conducted by Ashrof has revealed that all structural types of olefins can be hydroxylated using silver succinate and iodine in dry benzene medium. Silver succinate-iodine complex was prepared by reacting equimolecular amounts of silver succinate and iodine in dry benzene. The product of the reaction of silver succinate-iodine complex with typical aliphatic and aromatic terminal olefins, 1, 2-disubstituted ,

tri substituted, tetra substituted and cyclic olefins were investigated in detail and a mechanism was proposed for the hydroxylation which incorporated a general structure **1** for the intermediate involved.



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The present investigation was aimed at finding whether silver salts of some optically active derivatives of succinic acid can be used in place of silver succinate, along with iodine to achieve asymmetric dihydroxylation of olefinic compounds.

Another objective of the present work was to investigate on modifications of Woodward-Prevost reactions by the use of less expensive and more readily available metal carboxylates in place of silver carboxylates. The dihydroxylation of olefins using the Prevost's or woodward's method involves the use of silver carboxylates and halogen. The syn-hydroxylation from the more hindered face can be effected using Woodward's procedure in which olefins are treated with iodine and silver acetate in acetic acid. On the other hand, in the Prevost method, anti-dihydroxylation of olefin is generally achieved using iodine and silver benzoate in absence of water. Silver carboxylates have the disadvantages of being expensive, frequently unstable and difficult to dry.

Raman and Ashrof have shown that lead acetate may be used in the place of silver acetate in the Woodward's procedure for hydroxylation of octadec-cis-9-enoic acid (oleic acid).The present work involves investigations on the general applicability of this reagent for the hydroxylation of olefinic compounds and the mechanistic aspects of such reactions including the intermediate(s) involved.

2. Brief outline of the present study

i) Preparation of silver salt of optically active derivative of succinic acid from L-(+)- tartaric acid.

ii) Attempts towards the asymmetric dihydroxylation of olefinic compounds using this reagent.

iii) Dihydroxylation of olefinic compounds using lead acetate and iodine in wet acetic acid medium.

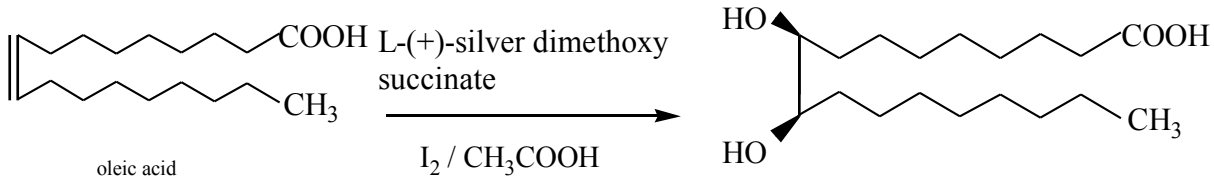
iv) Isolation and purification the intermediate involved in the dihydroxylation of olefins using this reagent.

v) Characterization of the intermediate by chemical, chromatographic and spectroscopic methods.

3. Brief account of the results and discussion

3.1 Asymmetric dihydroxylation of olefins using L-(+)-silver dimethoxy succinate and iodine.

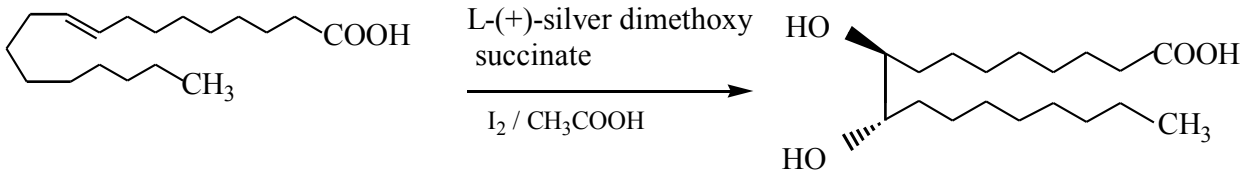
The starting material selected for preparing optically active derivative of succinic acid was obviously the naturally occurring optically active dicarboxylic acid, viz., tartaric acid. The naturally occurring L-(+)- tartaric acid was esterified and the hydroxyl groups of the diethyl ester were then methylated following the method of Purdie and Irvine. The diethyl dimethoxy succinate thus obtained was hydrolysed to get L-(+)- dimethoxy succinic acid. The silver salt of L-(+)- dimethoxy succinic acid was used along with iodine for the asymmetric dihydroxylation of olefinic compounds. Three olefinic fatty acids, viz., octadec-cis-9-enoic (oleic), octadec-trans-9-enoic (elaidic) and octadec-cis-6-enoic (petroselenic) acids were subjected to asymmetric dihydroxylation using L-(+)-silver dimethoxy succinate and iodine (scheme 1-3) by employing the procedure analogous to that used in silver succinate-iodine method.



oleic acid

octadec-cis-9 enoic acid (Oleic acid) erythro- 9, 10- dihydroxy stearic acid

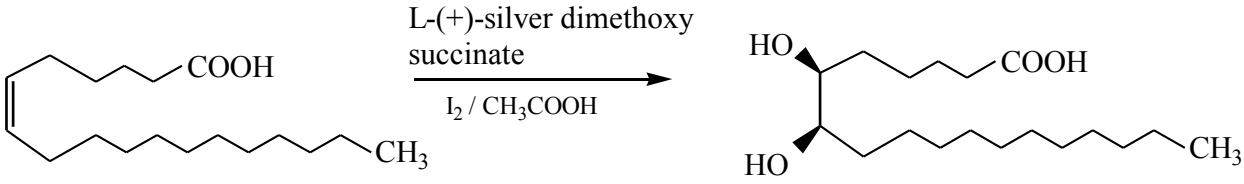
Scheme 1



octadec-trans-9-enoic acid Threo-9, 10-dihydroxy stearicacid

(Elaidic acid)

Scheme 2



octadec- cis-6-enoic acid Erythro-6, 7-dihydroxy stearic acid

(Petroselenic acid)

Scheme3

The 1, 2-diols obtained were characterized by mixed melting points, ^{1}H NMR, ^{13}C NMR and IR spectral techniques. In all cases the products of hydroxylation were found optically active.

3.2 Dihydroxylation of olefins using lead acetate and iodine.

Raman has described a method for hydroxylation of erucic acid (docos-cis-13-enoic acid) to 13, 14-dihydroxy docosanoic acid using silver acetate and iodine in wet acetic acid medium. A similar procedure was adopted in the present work for hydroxylating olefinic compounds using lead acetate and iodine. Several olefinic compounds comprising 1, 2-disubstituted, tri substituted and cyclic olefinic compounds were subjected to dihydroxylation using lead acetate and iodine. In all cases studied, where stereochemistry is relevant, syn-hydroxylation occurred. Thus the reagent can hydroxylate cis-olefinic fatty acids to the corresponding erythro-dihydroxy acids and, trans-acids to the corresponding threo-dihydroxy acids.

Presence of water has been reported to influence the products of hydroxylation by Woodward's procedure. Hence attempt was made to investigate the effect of moisture in the hydroxylation of olefins using lead acetate and iodine. The study revealed that, unlike in Woodward's reaction, dihydroxylation using lead acetate and iodine can be accomplished only in presence of water.

3.3 Analytical studies on the mechanistic aspects including the intermediate(s) involved in hydroxylation of olefins using lead acetate and iodine.

The product of reaction of lead acetate and iodine with ethyl oleate was investigated in detail in an attempt to characterize the intermediate of this hydroxylation reaction and to assign a mechanism for the syn-hydroxylation by the reagent. The intermediate was obtained by heating ethyl oleate with lead acetate, iodine and acetic acid containing water. It was purified and separated into fractions using column chromatography. Analysis by chemical and IR spectral techniques revealed that the intermediate involved is mainly the 9, 10-diacetoxy ethyl stearate along with small amounts of the iodoacetae. The presumed intermediate was synthesised by standard methods and its IR spectrum was found super imposable with that of the intermediate isolated. Accordingly, a mechanism has been proposed for the dihydroxylation of olefins using lead acetate and iodine. The dihydroxylation by lead acetate and iodine is found to operate by a mechanism different from that of Woodward, Prevost and silver succinate-iodine methods of hydroxyltion of olefinic compounds..

4. Conclusions

L-(+)-silver dimethoxy succinate and iodine in benzene medium is shown to be an effective reagent for accomplishing asymmetric synthesis of 1,2-diols from olefinic compounds by dihydroxylation. The development of L-(+)-silver dimethoxy succinate and iodine as a syn-hydroxylating agent also amounts to yet another extension of the well known Prevost-Woodward methods. Lead acetate and iodine in 'wet' acetic acid medium is also proved to be a simple and effective reagent for stereospecific dihydroxylation of olefinic compounds. The dihydroxylation by lead acetate and iodine is found to operate by a mechanism different from that of Woodward, Prevost and silver succinate-iodine methods.

5. Organisation of the thesis

Chapter 1. dihydroxylation of olefinic compounds – A concise Review

A review on the important methods of effecting cis- and trans-dihydroxylation of olefinic compounds.

chapter 2. asymmetric synthesis of Diols- An overview

A brief account of the methods currently available for the asymmetric synthesis of 1, 2-diols from olefinic compounds.

Chapter 3. Asymmetric dihydroxylation of olefins using L-(+)-silver dimethoxy succinate and iodine.

i) Synthesis of L-(+)-silver dimethoxy succinate starting from L-(+)- tartaric acid.
ii) Asymmetric dihydroxylation of octadec-cis-9-enoic (oleic), octadec-trans-9-enoic (elaidic), and octadec-cis-6-enoic (petroselenic) acids using L-(+)-silver dimethoxy succinate and iodine.

Chapter 4. Dihydroxylation of olefins using lead acetate and iodine.

Dihydroxylation of olefinic compounds of several types comprising 1, 2-disubstituted, tri subtituted and cyclic olefins using lead acetate and iodine.

Chapter 5. Analytical investigations on nature of the intermediate involved in dihydroxylation of olefinic compounds using lead acetate and iodine.

i) Isolation and purification of the intermediate(s) involved in dihydroxylation of ethyl oleate using lead acetate and iodine.

ii) Characterization of the intermediate by chemical, chromatographic and spectroscopic techniques.